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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,743	12/12/2000	Wei-min Liu	3298.1	7518

22886 7590 09/16/2005

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EXAMINER

ALLEN, MARIANNE P

ART UNIT PAPER NUMBER

1631

DATE MAILED: 09/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/735,743

Applicant(s)

LIU ET AL.

Examiner

Marianne P. Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-21, 23-34, 36-47, 49-59, 61-72, 74-85, 87-97, 99-103 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 26-34, 36-38, 64-72, 74-76, 90, 102 and 103 is/are allowed.
- 6) ☒ Claim(s) 1, 39 and 77 is/are rejected.
- 7) ☒ Claim(s) 2-9, 11-21, 23-25, 40-47, 49-59, 61-63, 78-85, 87-89, 91-97, and 99-101 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant filed an appeal brief on 6/24/2005. This appeal brief was non-compliant for at least the reason that the concise explanation of the subject matter defined in the independent claims did not refer to page and line numbers of the specification. However, review of the appeal brief also revealed that the claims listed as being finally rejected and under appeal did not match the claims rejected in the various grounds of rejection. This inconsistency was also present in at least the final rejection mailed 11/24/04 where the claims listed as rejected on the cover sheet do not match those rejected in the various grounds of rejection. As such, finality of this Office action is hereby reopened to clarify the record. The examiner has reviewed the specification, art of record, and rejections of record and has considered the arguments presented in the appeal brief. Upon further consideration, all rejections under 112, 1st and 2nd paragraph, will be withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1, 39, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (1996) in view of either Hogg et al. or Hollander et al.

Lockhart et al. discloses quantitative analysis of the signal intensity of PM and MM pairs from an array hybridization experiment. The results are used to make a determination of the presence or absence of a nucleic acid. The average of the logarithm of the PM/MM ratios for each probe set is computed along with the number of instances in which the PM hybridization signal is larger than the MM signal. The decision matrix used is not disclosed. The quantitative

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analysis is performed on a computer system using appropriate software. (See page 1679.) The reference does not disclose calculating a p -value using a Wilcoxon's signed rank test. It is noted that this work is cited as known prior art in the instant specification at page 17.

Hogg et al. and Hollander et al. disclose the Wilcoxon's signed rank test and its use for non-parametric data. It is noted these references are cited as known prior art in the instant specification at page 22.

One of ordinary skill in the art would have been aware that hybridization data from nucleic acid arrays could be treated as nonparametric data. A parametric test assumes the data was from a population that follows a Gaussian or normal distribution. A nonparametric test does not assume a particular distribution of data. Using nonparametric statistics would have been well known in the nucleic acid arts and expression analysis with respect to differences in signal intensity. See at least Lynch et al. (U.S. Patent No. 5,988,139 at column 9, lines 44-51), Chartier-Harlin et al. (U.S. Patent No. 6,391,553 at column 8, lines 38-53), Kargman et al. (U.S. Patent No. 6,593,361 at column 15, line 67, through column 16, line 30) as evidence that those of ordinary skill in the art would have understood the applicability of nonparametric statistics, including Wilcoxon's signed rank test, in this area of technology. See also the reference to Chen et al. (Journal of Biomedical Optics, October 1997) submitted by applicant. Microarray intensity data is compared using the nonparametric Mann-Whitney test in ratio-based decisions and quantitative analysis of cDNA microarrays using hybridization intensities. As such, it would have been obvious to use known nonparametric statistical analysis to analyze the results of multiple probe experiments for perfect match and mismatch probes. Lockhart et al. discloses a method for determining the presence or absence of a nucleic acid using signal information from

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PM and MM hybridization signals. It would have been obvious to use the difference between the PM and MM signals for each probe set as the test statistic in the Wilcoxon's signed rank test to determine presence or absence of the nucleic acid. Such statistical analysis would have been routinely performed using computer systems and appropriate software.

Applicant's arguments regarding lack of basis for asserting that hybridization data would be appropriate for use in non-parametric statistical analysis is not persuasive.

Conclusion

Claims 26-34, 36-38, 64-72, 74-76, 90, and 102-103 are allowable.

Claims 2-9, 11-21, 23-25, 40-47, 49-59, 61-63, 78-85, 87-89, 91-97, and 99-101 are objected to as depending upon a rejected base claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Marianne P. Allen

Marianne P. Allen
Primary Examiner
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9/14/05

mpa